

## RESPONSE

### **I. Status of the Claims**

No claims have been cancelled. No claims have been amended. No new claims have been added.

Claims 1-3 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**.

### **II. Rejection of Claims 1-3 Under 35 U.S.C. § 101**

The Action first rejects claims 1-3 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

As set forth in Applicants' response filed on October 7, 2002 ("the previous response") to the First Office Action in the present case, which was mailed on July 8, 2002, the present invention has a number of substantial and credible utilities, not the least of which is in forensic analysis, as described in the specification, at least at page 4, line 31, page 36, lines 30-31, and page 38, lines 4-5. As described in the specification at page 8, lines 25-28, the present sequences define a coding single nucleotide polymorphism - specifically, a G/A polymorphism at position 146 of SEQ ID NO:8, which can lead to a serine or asparagine residue at amino acid position 49 of SEQ ID NO:9. As such polymorphisms are the basis for forensic analysis, which in undoubtedly a "real world" utility, the present sequences must in themselves be useful.

The Action states that the use of the present sequences in forensic analysis is not a specific utility because "there is no specific disclosure of the population(s) that the sequence can distinguish" (Action at page 5). Applicants respectfully point out that the presently described polymorphisms are useful in forensic analysis exactly as they were described in the specification as originally filed - specifically, to specifically identify individual members of the human population based on the presence or absence of the described polymorphism. Simply because the use of these polymorphic markers will necessarily provide additional information on the percentage of particular subpopulations that contain one or more of these polymorphic markers does not mean that "additional research" is needed in order for these markers as they are presently described in the

instant specification to be of use to forensic science. Thus, the Examiner's position does not support the alleged lack of utility. As stated above, using the polymorphic markers as described in the specification as originally filed will definitely distinguish members of a population from one another. In the worst case scenario, each of these markers are useful to distinguish 50% of the population (in other words, the marker being present in half of the population). The ability to eliminate 50% of the population from a forensic analysis clearly is a real world, practical utility. Therefore, the allegation that the use of the presently described polymorphic markers is only potentially useful is without merit, and does not support the alleged lack of utility.

As set forth in the previous response, it is important to note that the presence of other or more useful polymorphic markers for forensic analysis does not mean that the present sequences lack a specific utility. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991):

An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Just because other polymorphic sequences from the human genome have been described does not mean that the use of the presently described polymorphic markers for forensic analysis is not a specific utility. The Examiner seems to be confusing the requirement for a specific utility, which is the proper standard for utility under 35 U.S.C. § 101, with that of a unique utility, which is clearly an improper standard. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, just to name a few particular examples, because examples of each of these have already been described and patented. However, only the briefest perusal of any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the

requirements of 35 U.S.C. § 101.

Additionally, as set forth in the previous response, a sequence sharing over 99% percent identity at the amino acid level over the entire length of the described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as “Homo sapiens gene for seven transmembrane helix receptor” (GenBank accession number AB065623). The Action states that “there is no sufficient and credible information that indicates the published sequence is a functional GPCR” (Action at page 3). Applicants point out that an additional sequence sharing over 99% percent identity at the amino acid level over the entire length of the described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by different third party scientists *wholly unaffiliated with Applicants* as a “G-protein coupled receptor” (GenBank accession number BD144530). The alignment of these sequences is shown in **Exhibit B** (query is SEQ ID NO:9). The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given these two GenBank annotations, there can be no question that those skilled in the art would clearly believe that Applicants’ sequence is a G-protein coupled receptor. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

As 60% of the pharmaceutical products currently being market by the entire industry target G-protein coupled receptors (Gurrath, 2001, Curr. Med. Chem. 8:1605-1648), a preponderance of the evidence clearly weighs in favor of Applicants' assertion that the skilled artisan would readily recognize that the presently described sequences have a specific (the claimed GPCR proteins are encoded by a specific locus on the human genome), credible, and well-established utility, for example in tracking gene expression. As set forth in the previous response, as taught in the specification as originally filed, at least at page 10, lines 13-16, the claimed polynucleotide sequences can be used to track the expression of the gene encoding the described protein. In particular, the specification describes how the described sequence can be represented using a gene chip format to provide a high throughput analysis of the level of gene expression. Such “DNA chips” clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. As the present

sequences are specific markers of the human genome (see below), and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such DNA chips. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful.

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, two such companies (Agilent acquired by American Home Products and Rosetta acquired by Merck) were viewed to have such "real world" value that they were acquired by large pharmaceutical companies for significant sums of money. The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, *Science* 291:1304). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, *Science* 291:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years). Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Although Applicants need only make one credible assertion of utility to meet the

requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, as described in the specification at least at page 4, lines 24-26, the present nucleotide sequences have a specific utility in mapping a unique gene to a particular chromosome. This is evidenced by the fact that SEQ ID NO:8 can be used to map the presently claimed sequence to chromosome 1 (present within the chromosome 1 clone, Genbank Accession Number AC091612; alignment and the first page from the Genbank report are presented in **Exhibit C**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 1 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Applicants respectfully remind the Examiner that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence, as described above. Applicants respectfully submit that the practical scientific value of biologically validated, expressed and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants' position, the Examiner is requested to review, for example, section 3 of Venter *et al.* (*supra* at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the

requirements of 35 U.S.C. § 101.

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office (“the PTO”) itself for compliance with 35 U.S.C. § 101. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the “real-world” utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section III, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, as well as the reasons set forth in Applicants’ response filed on October 7, 2002 to the first Office Action mailed on July 8, 2002, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific,

credible and well-established utility, the rejection of claims 1-3 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

**III. Rejection of Claims 1-3 Under 35 U.S.C. § 112, First Paragraph**

The Action next rejects claims 1-3 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1-3 have been shown to have "a specific, substantial, and credible utility", as detailed in section II above, the present rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, be withdrawn.

**IV. Conclusion**

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Li have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

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Date

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